Over 100 medications have been reported to cause acute pancreatitis, generally in isolated case reports. None have been postulated to cause chronic pancreatitis with necrosis. An 84-year-old woman presented with syncope after sudden onset of non-bloody emesis and mid-abdominal pain for five hours. She was afebrile with a blood pressure of 121/66 and found to have serum lipase > 4000 U/l. Computer tomography scan (CT) with contrast was consistent with pancreatitis and showed an obstructive picture with intrahepatic and common bile duct dilatation. Her surgical history was significant for cholecystectomy over 20 years ago. She denied alcohol use but had been taking sulindac 200mg twice daily and hydrochlorothiazide 12.5mg daily for over 6 years, and had started lisinopril 10 mg daily one year ago. She described one episode of milder but similar sharp abdominal pain 6 years ago that resolved spontaneously. Imaging done at the time had revealed a dilated common bile duct without gallstones, but no etiology was found on subsequent workup. Initially the patient’s Ranson’s criteria predicted a 2% mortality. Her home medications were held and she received supportive care.

Assessment

On the first hospital day, she became febrile and deteriorated rapidly with ileus and increasing hypoxia with new onset atrial fibrillation. Repeat CT scan of the abdomen showed necrotizing pancreatitis (Figure 1). Her 48-hour Ranson’s criteria predicted a 15% mortality. The patient was started on IV meropenem and was transferred to the intensive care unit. In this patient’s case, the finding of a dilated common bile duct in the absence of a gallbladder limited the cause to papillary stenosis, gallstone obstruction in other parts of the biliary tract, and medication. A magnetic resonance cholangiopancreatography was negative for any obstruction or sphincter abnormalities. Thus, we propose this patient’s chronic pancreatitis resulted from repeated subclinical drug-induced acute pancreatitis which predisposed her to increased risk of necrotizing pancreatitis when a third insult, lisinopril, was added to her medications.

Discussion

We report a case of necrotizing pancreatitis with progression to chronic pancreatitis following concurrent use of three implicated medications, including sulindac (Clinoril; Merck Sharp & Dohme, West Point, Pennsylvania), hydrochlorothiazide, and lisinopril. Though drug-induced pancreatitis is rare, hydrochlorothiazide and lisinopril are frequently prescribed antihypertensives with a variable latency period and documented severe cases of necrotizing pancreatitis. The proposed mechanism for lisinopril and hydrochlorothiazide is hypotension and pancreatic ischemia. Only 15% of acute pancreatitis cases develop into necrotizing pancreatitis, which has a mortality that is three times that of acute pancreatitis (17%). Sulindac has been implicated in numerous cases of acute pancreatitis with a latency period as long as five years between ingestion and clinical presentation. Its clinical presentation resembles gallstone pancreatitis in the

Figure 1. Computer tomography scan with intravenous contrast demonstrating necrotizing pancreatitis. New nonenhancing area in proximal body superimposed on edematous pancreas consistent with known acute pancreatitis does not indicate any discrete drainable fluid collection.

Figure 2. Magnetic resonance imaging with contrast revealing 11x7cm non-enhancing cystic lesion within the body of the pancreas corresponding to a pancreatic pseudocyst with internal debris. Additional small cystic lesions in pancreatic tail likely represent additional smaller pseudocysts and areas of pancreatic ductal dilatation.
absence of stones, which may explain the patient’s biliary duct and intrahepatic dilatation on initial CT scan which is reversible with the cessation of sulindac. The proposed mechanism is sulindac metabolite deposition in biliary epithelial cells and inhibition of canalicular bile transport, leading to hypercholesterolemia.5

Supportive care is the mainstay of treatment. The patient received IV antibiotics, IV fluids and pain medication. Other than an episode of rapid atrial fibrillation, the patient did not have any other complications. Seven days post admission the patient was discharged to home. Two weeks later, the patient returned with fever, abdominal pain, and constipation and was diagnosed with chronic pancreatitis. Imaging revealed a new 11 cm pseudocyst obstructing the splenic vein and narrowing of the portal vein (Figure 2). She was treated supportively and discharged with outpatient follow-up for drainage in two to three weeks.

Gallstones, alcohol, and hypertriglyceridemia were ruled out in our patient prior to diagnosing drug-induced pancreatitis. The necrosis-fibrosis concept describes chronic pancreatitis as progressive inflammatory damage and fibrosis resulting from repeated episodes of acute pancreatitis.6 The majority are alcohol related, and there have been no established cases linked with medications. The literature has reported a few case reports of different medications causing fatal pancreatitis including sulindac, hydrochlorothiazide and lisinopril,1,4 although ours is the first case to report chronic pancreatitis in a patient on all three medications. Clinicians should consider medications in patients with gastrointestinal complaints, especially in those with pancreatitis that is not caused by gallbladder disease or alcohol use.

**REFERENCES**


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The authors and or spouses/significant others have no financial interest to disclose.

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